Attorney Docket No.: DEX-0180
Inventors: Roberto A. Macina
Serial No.: 09/806,302
Filing Date: July 19, 2001
Page 7

REMARKS

Claims 1-10 are pending in the instant application. Claims 7-10 have been withdrawn form consideration by the Examiner and subsequently canceled by Applicant in this amendment. Claims 1-6 have been rejected. Claims 1 through 5 have been amended. Support for the amendments is provided in claim 6 which is now canceled. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Finality of Restriction Requirement

The Examiner has made final the Restriction Requirement mailed October 1, 2002. Thus, in earnest effort to facilitate the prosecution of this case, Applicant has canceled without prejudice non-elected claims 7-10. However, in light of the finality of this Restriction Requirement, Applicant reserves the right to file a divisional application to the canceled subject matter.

II. Rejection of Claims 1, 3, 5-6 under 35 U.S.C. § 112, first paragraph

Claims 1, 3, 5 and 6 (to the extent is depends from claims 1, 3 or 5) have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described

Received from < 8568101454 > at 8/11/03 3:53:50 PM [Eastern Daylight Time]

in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner suggests that claims 1, 3, 5 and 6 are not enabled by the specification because the specification fails to establish that measuring either SEQ ID NO:1 or SEQ ID NO:2 may be used to diagnose a gynecologic cancer, stage a gynecologic cancer or monitor a change in stage of a gynecologic cancer. In particular, the Examiner has questioned the predictiveness of data presented in the specification demonstrating that overexpression of ESBPIII was detected in 6 out of 11 samples. Further the Examiner suggests that one of skill would be unable to predict from these data that measuring levels of ESBPIII could be used to assess a stage or to monitor a change in stage of gynecologic cancer, because the data in Table 2 does not classify the samples by cancer stage. In addition, the Examiner suggests that claims 1, 3, 5 and 6 are not enabled by the specification to the extent that the claims read on using measurements of protein levels as a basis for a method for diagnosis, staging or monitoring a change in cancer stage.

Applicant respectfully traverses this rejection.

At the outset, Applicant respectfully disagrees with the

Received from < 8568101454 > at 8/11/03 3:53:50 PM [Eastern Daylight Time]

Examiner's suggestion that the predictive power of data such as provided for SEQ ID NO:1 showing that greater than 50% of gynecologic cancer samples exhibited elevated levels of SEQ ID NO:1 does not provide a basis for a diagnostic test of gynecologic cancers. The specificity/sensitivity of this marker is actually greater than many useful cancer therapeutics and diagnostics that have been FDA approved and are commercially available. For example, Genentech's product Herceptin and its diagnostic counterpart, the HercepTest are very successful commercially. Yet many publications show the relevant gene, HER-2, is overexpressed in 30% of breast cancer patients. Hence, the specificity and sensitivity of the ESBPIII claimed in the instant application is clearly sufficient for predictable diagnostic and monitoring uses with gynecologic cancers.

Further, as set forth in MPEP § 2164.03, the predictability or lack thereof in an art field refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. Results evidencing the utility of ESBPIII of the present invention as a diagnostic marker for gynecologic cancers is presented in the specification beginning at page 16. Those of skill in the art routinely extrapolate data relating to specificity of markers, such as provided for ESBPIII

Received from < 8568101454 > at 8/11/03 3:53:50 PM [Eastern Daylight Time]

in gynecologic tissue, to be indicative of metastasis and/or advanced stages of gynecologic cancers when an increase in these markers is detected in cells, tissues or bodily fluids other than gynecologic tissues. Thus, contrary to the Examiner's suggestion, the claimed invention for metastasis and staging is predictable when read in light of the teachings of the specification which clearly provide one skilled in the art with the ability to extrapolate the disclosed results to the claimed invention. FDA approved commercially available products such as HercepTest also indicate that development of a diagnostic assay based upon data such as provided in the instant application is routinely performed by those skilled in the art.

MPEP § 2164 sets forth the enablement requirement of 35 U.S.C. § 112, first paragraph. The enablement requirement refers to the requirement of 35 U.S.C. § 112, first paragraph that the specification describe how to make and how to use the invention. The invention that one skilled in the art must be enabled to make and use is defined by the claim(s) of the particular application. The instant specification provides the sequence information for ESBPIII of the present invention as well as detailed methodologies for measuring ESBPIII levels in a patient. See pages 11-14. The specification also provides detailed

Received from < 8568101454 > at 8/11/03 3:53:50 PM [Eastern Daylight Time]

methodologies for use of these markers to diagnose (see pages 8-10 of specification), stage (see page 10 of specification) and monitor (see page 10-11 of specification) gynecologic cancers in patients. Further, as discussed in detail above, the instant specification also provides data understood by the skilled artisan to be demonstrative of the ESBPIII being diagnostic for gynecologic cancers as claimed. Accordingly, the instant specification clearly teaches one of skill in the art how to make and use the invention as claimed.

Applicant also respectfully disagrees with the Examiner suggestion that the specification is not predictive of a method for measurement of protein levels as well. The literature references relied upon the Examiner to suggest that steady state levels of proteins does not necessarily correlate to steady state levels of mRNA, namely Shantz and Pegg (Int. J. of Biochem. and Cell Biol. 1999 31:107-122), McClean and Hill (Eur. J. Cancer 1993 29A:2243-2248) and Fu et al. (EMBO Journal 1996 15:4392-4401) are reporting unique findings of scientific interest wherein researchers unexpectedly found that protein and mRNA levels did not always correlate for a unique group of proteins. These three references relating to three unique proteins, none of which serve as cancer markers for gynecologic cancers as in the

Received from < 8568101454 > at 8/11/03 3:53:50 PM [Eastern Daylight Time]

present invention, are hardly representative of the art for proteins in general wherein mRNA levels correlate quite well with protein levels. Much more relevant are the recent teachings of Lopez-Guerrero et al. (Arkh Patol. 2003 65(1):50-5 (Abstract copy provided herewith) reporting a 93-95% correlation between protein and mRNA levels for the diagnostic breast cancer marker HER-2 detected in the commercially available HercepTest. The commercially available HercepTest, as well as the teachings of Lopez-Guerrero et al., demonstrate the ability of those skilled in the art to extrapolate results such as those disclosed in the instant specification relating to ESBPIII mRNA expression levels to the claimed invention wherein protein levels can also determined. Accordingly, further demonstration in the specification with respect to predictability of protein level determination is not required.

It is respectfully requested that this rejection under 35 U.S.C. § 112, first paragraph, be withdrawn in light of the above remarks and amendments to the claims.

III. Rejection of Claims 2, 4 and 6 under 35 U.S.C. § 102(e)

Claims 2, 4 and 6 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Lehrer. The Examiner suggests that Lehrer teaches methods comprising measuring lipophilin c,

Received from < 8568101454 > at 8/11/03 3:53:50 PM [Eastern Daylight Time]

which is a protein that has the same amino acid sequence as that of SEQ ID NO:2, and is therefore, encoded by SEQ ID NO:1. The Examiner suggests that Lehrer teaches that measuring levels of lipophilin c could be used to detect metastasized cells and that lipophilin c is expressed in uterus, breast and ovary. Finally, the Examiner suggests that Lehrer teaches methods of detection of metastasis of gynecologic cancer that are the same as claimed.

Applicant respectfully traverses this rejection.

The only teachings in Lehrer relevant to detection of ESBPIII in cancerous tissue are set forth in Example 8, paragraph 0073, and are related to prostate cancer cells. All other teachings in Lehrer regarding expression of this protein in tissue types such as testis, uterus, breast and ovary are in normal cells and are not predictive nor enabling of expression of this protein in cancer cells. Thus, unlike the instant application wherein expression in cancer tissue samples was specifically examined, the teachings of the Lehrer reference do not enable detection of metastasis of gynecologic cancers and therefore cannot anticipate the claimed invention.

Withdrawal of this rejection under 35 U.S.C. § 102(e) is therefore respectfully requested.

Received from < 8568101454 > at 8/11/03 3:53:50 PM [Eastern Daylight Time]

IV. Conclusion

Applicant believes that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

Kathleen A. Tyrrell
Registration No. 38,350

Date: August 11, 2003

LICATA & TYRRELL P.C.
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515

Received from < 8568101454 > at 8/11/03 3:53:50 PM [Eastern Daylight Time]

NCBI PubMed National Library of Medicine NLM

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM

Search PubMed for

Limits Preview/Index History Clipboard Detail

About Entrez

Abstract Show: 20 Sort Text

Text Version

Entrez PubMed
Overview
Help | FAQ
Tutorial
New/Noteworthy
E-Utilities

PubMed Services
Journals Database
MeSH Database
Single Citation Matcher
Batch Citation Matcher
Clinical Queries
LinkOut
Cubby

Related Resources
Order Documents
NLM Gateway
TOXNET
Consumer Health
Clinical Alerts
ClinicalTrials.gov
PubMed Central

Privacy Policy

1: Arkh Patol. 2003 Jan-Feb;65(1):50-5. Related Articles, L

Histological tumor grade correlates with HER2/c-erB-2 status invasive breast cancer: a comparative analysis between immunohistochemical (CB11 clone and Herceptest), FISH and differential PCR procedures.

Lopez-Guerrero JA, Navarro S, Noguera R, Almenar S, Pellin A, Vazquez C, Llombart-Bosch A.

Department of Pathology, School of Medicine, University of Valencia, Spa

There is a growing clinical demand for analysis of the HER2/c-erbB-2 (HER2) status of breast cancer specimens because it provides valuable prognostic, predictive and therapeutic information. In this sense, a variety methods is available for detection of HER2 status, although to date a reliab and sensitive test does not exist. In order to choose the most suitable procedure to assess HER2 status, we analyzed 102 invasive breast cancers HER2 overexpression by means of immunohistochemistry (IHC), with the CB11 Mo-Ab and the Hercep Test kit, and for HER2 gene amplification b fluorescence in situ hyubridization (FISH) and differential PCR (dPCR). HER2 overexpression, determined by CB11 (group C) and HercepTest (2+ and 3+), was observed in 19 samples (18.6%) whereas genetic amplificatio was detected in 31 (30.4%) and 14 (13.7%) cases by FISH and dPCR, respectively. The majority of overexpressed/amplified specimens corresponded to high grade tumors. We found concordances of 78-80% an 93-95% between IHC vs FISH and IHC vs dPCR, respectively. Considerin FISH procedure as a gold standard, we found a sensitivity and specificity o 48.4% and 94.3% for CB11 antibody, of 45.2% and 92.9% for HercepTest, and of 45.2% and for 100% for the dPCR. Thus, considering the sensitivity specificity and the high grade of concordance between IHC and dPCR, we suggest the use of IHC for assessing HER2 status. However, due that sensitivity of IHC test is lower than FISH, we also suggest to carry out FIS on those cass in which IHC results are not definitive for its clinical evaluati

PMID: 12669615 [PubMed - in process]

Abstract Show: 20 Sort Text